November 20, 1951

Dr. Francis J. Ryan
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Dear Francis:

I hope that by now you may have dug deeply enough into the work awaiting you on your return that you can attend to some ordinary correspondence. Esther and I are sure that your trip must have been a great success. Aside from the envy they excited, we found great pleasure in the accounts you returned to Columbia of the earlier, South American part of your odyssey. Alain Bussard told us that you were occupying one of his apartments while he was here at Madison. We trust you enjoyed Paris as much as we enjoyed Alain.

The pretence for this letter is to ask you whether you have any recollection of or legible notes on heterokaryons of leucineless Neurospora with other auxotrophic mutants. As far as I can make out from my own notes, marked combinations of 33757 with 4545 became pure L-, even on minimal medium. However, my records are very skimpy (as were these particular experiments), and I hoped you might be able to add to them. In view of the frequency with which L+ was eliminated by L-, even on minimal agar, the indicated result is the expected one, but I would enjoy a confirmation of the experiment. It has been a long time since I've looked at these notes, or thought about Neurospora -- the present occasion is simply for an incidental detail in a review article. Looking over the notes, the problem of selection in the heterokaryon seems to me no less interesting than ever. Have any of your students at Columbia done any more with it? For example, with the usual L+ and L-, the heterokaryon is, of course, quite unstable on minimal medium, and may go either way. One of the 15300 albino stocks, however, was "immune" to the selective action of L-, but these heterokaryons persisted, losing neither L+ nor L- on minimal. I should think that natural selection in heterokaryons could answer some questions on the sites of gene action.

I would be eager to exchange notes with you on the Parisian trip. Even with Cohn and Monod, transatlantic communications have not been as facile as either of us would hope, and all I've heard about your own activities has been some hints from Kim. I do hope we will have some such opportunity before too long, but after the Cold Spring Harbor meetings last June (and a quick trip to Minneapolis) we're not eager to go to any more meetings. But look who's talking about trips!

After a long period of concentration on details of K-12 (which have sometimes seemed like fleas we were straining at) the lab is going off in what seems like all directions. I hope we will get things under control again before too long, but it looks to be unlikely until some long-awaited but unmaterialized new space becomes available. As a physicist friend put it, we have more square people per foot than anybody. If I get going on this, as you know, I'll end up with another 60 p. manuscript.

Esther is working in the lab. next to me-- got her Ph.D. about the time you left last year; her thesis was on the genetics of reverse-mutation at the Lac$_I$ locus, and the interesting allelic relationships there. One of the points she went into briefly was the selection of Lac- mutants with butyl galactoside. Kim wasn't too clear about this, but we gathered you were following a similar lead while you were at the Institut Pasteur. We didn't do a great deal with this, and would like to compare notes with you on it. Since then she's been working out the genetic relationships of lysogenic and sensitive forms, etc., in K-12. Make what you will of this, but the difference segregates in crosses, and heterozygous diploids, as if the types result from different alleles at a mappable locus, rather than cytoplasmic infection. Her studies on the infection of sensitive bacteria also suggest something more complex than the usually assumed random fraction of infected bacteria becoming promptly lysogenic.

You will remember sending Norton Zinder here. He has changed a good deal (including a wife and child) but is still recognizable. After a slow start on what may have seemed a dull problem, he is finishing up a competent thesis on a fascinating system: the "genetic transductions" in Salmonella, which I would never believe in any detail except for seeing them in hand. The latest item on this (since the note in MGB) is carrying over a flagellar antigen from S. typhimurium to S. typhi to create a "serological hybrid": IX, XII, i --. This would certainly have been called a new "species" if it had been picked up from a gut. Norton developed a miniature Neurospora growth tube to study the migrations of flagellar types in serum agar. Nothing more very definite on the (hel)L-forms. He's finishing and writing up his work now, to get out in June, and looking for a job.

Nort.'s my only regular Ph.D. student at the moment. Ethelyn Lively is continuing her cytological and starting well into cell-pedigree work. Another girl is picking holes (mostly loopholes) in our K-12 linkage map, but the strategic features hold up. Elisa Cahn (ex Davis' lab; CSH) has just started, on nothing much in particular so far. A postdoctoral, Dave Skaar (ex Sonneborn) is working on serology, interstrain crosses, and some miscellany. About the same applies to myself, what with some teaching (bacterial genetics) this year. But I get a fond recollection of Neurospora work with a new line on actinomycetes (Streptomyces griseus) which handles very well for biochemical mutants (especially with replica plating, which should also work for sorbose-inhibited Neurospora as well as bacteria generally). With waiting 2-3 days for growth, perhaps life can be relaxed again. This work has just begun: three guesses what I'm after.

You must remember my brother Seymour. He's a graduate student now at Illinois more or less with Luria. He just wrote (God forfend) that he might be interested in lysogenicity: you may yet see a paper by S. Lederberg that refers to work by E. and J. Lederberg (not to mention my 10-yr old brother Bernard). But all the Wollman's seem to have managed (in this respect) without too much pain.

Esthervand send our best to the Ryans. Welcome back, and say hello to Lil for us too.

Sincerely,

Joshua Lederberg